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08/728463

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/728,463	10/10/96	LONBERG	N 14643-009020

EXAMINER

HM12/0217

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ART UNIT	PAPER NUMBER
1644	21

DATE MAILED: 02/17/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 6/11/99; 10/29/99

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-10, 12-29, 31-53 is/are pending in the application.
Of the above, claim(s) 1-9, 15-17 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 10, 12, 13, 14, 18-29, 31-53 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

NOT ATTACHED W/ IDS
PAPER FILE NOT AVAILABLE.
USSN 08/352222 AT THIS TIME

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-404-496/40517

DETAILED ACTION

1. Applicant's amendment, filed 6/11/99 (Paper No. 16), has been acknowledged.
Claims 10-14, 18 and 22-30 were amended.
Claims 31-51 were added.

Applicant's amendment, filed 10/29/99 (Paper No. 20), is acknowledged.
Claims 11 and 30 have been canceled.
Claims 52-53 have been added.

As pointed out in the previous Office Action (Paper No. 14); it appears that the species comprising A-T comprising particular amino acids wherein the immunoglobulin is CD4-specific are free of the art. However there are issues under 112, first and second paragraphs as well as art on the generic claims, as indicated herein.

Claims 1-9 and 15-17 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 10, 12-14, 18-29, 31-53 are being acted upon as the elected invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 6/11/99 (Paper No. 16).
The rejections of record can be found in the previous Office Action (Paper No. 14).

3. As pointed out previously, all of the priority applications USSNs were not available to the examiner at this time.

Due to the number of CIPs in the priority applications, applicant is invited to indicate the written support and enablement under 35 USC 112, first paragraph, for the instant claims, including the non-elected species in the interest of compact prosecution.

In response to the prior art rejections of record, applicant has asserted priority for certain claims to certain priority dates. However, applicant has not provided sufficient direction or objective evidence to provide for the written support for the current claims to these priority documents.

4. Applicant's amendment, filed 6/11/99 (Paper No. 16), providing substitute pages for Tables 1,2,4 and 7 is acknowledged. Applicant states that the substitute pages filed contain no new matter.

5. Upon reconsideration of applicant's arguments and the support on page 257 in Table 1; the previous objection to the specification o as failing to provide proper antecedent basis for the claimed subject matter set forth in claim 22 has been withdrawn.

6. Claims 13 and 14, are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: ""similar affinity" and "at least about"

Applicant's amendment, filed 6/11/99 (Paper No. 16), directs support to pages 95-96 and 248-252 of the specification as filed for these "limitations", respectively.

However, the disclosure on pages 95-96 are drawn to structural similarity and do not appear to provide sufficient written description nor set forth the metes and bounds for "similar affinity" as currently encompassed by the claimed invention.

In addition, the disclosure on pages 248-252 do not provide sufficient written description nor set forth the metes and bound for "at least about"as currently encompassed by the claimed invention.

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed

7. Claims 13, 14, 22-29, 37, 40, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments, filed 6/11/99 (Paper No. 16), have been fully considered but are not found convincing. Applicant asserts that given the objective evidence in the specification as filed (e.g. Examples 40-41) that the 10 individual hybridomas (e.g. 1E11, 1G2, 6G5, 10C5, 1G1, 6C1, 2E4, 7G2, 1F8, 4D1) all generate antibodies that bind CD4. .

The issue is not whether the particular hybridomas produce CD4-specific antibodies, but rather immunoglobulins that comprise a limited or discrete sequence (e.g. SEQ ID NO:1, etc. etc. etc.) such as the claimed elements set forth in claims 13-14 and 22-30 would have the property of binding CD4. Applicant is invited to provide objective evidence that immunoglobulins comprising these particular elements do bind and are enabled for binding CD4. As pointed out previously, it was noted that certain sequences such as SEQ ID NO: 1 and SEQ ID NO:3 have been found in antibodies of specificities other than CD4. In the absence of objective evidence, there appears to be insufficient enablement for the scope of immunoglobulins that can bind CD4, that incorporate the particular amino acids or constructs as set forth in the instant claims.

Applicant's arguments are not found persuasive.

Applicant is invited to consider claiming CD4-specific human monoclonal antibodies with all of the appropriate sequences that provide for binding CD4.

8. Claims 35 and 38: It is apparent that the 1E11, 1G2, 6G5, 10C5, 1G1, 6C1, 2E4, 7G2, 1F8, 4D1 antibodies and hybridomas are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

9. Upon reconsideration of applicant's amended claims, the previous rejection with respect to the recitation of "substantially the same sequence" or "substantially identical to an amino acid sequence" has been withdrawn.

10. Claim 38 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Given that claim 38 is dependent on claim 35, which recites specific mononclonal antibodies; the recitation of claim 38 merely recites an inherent property of these specific monoclonal antibodies and do not further limit the claimed antibodies recited in claim 35.

11. Claims 13, 14, 35 and 38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Applicant's arguments, filed 6/11/99 (Paper No. 16), concerning the recitation of "artificial gene" is acknowledged; however the pending elected claims do not recite "artificial gene". Therefore, applicant's arguments are rendered moot.

B) Claims 13 and 14 are indefinite in the recitation of "similar affinity" because this phrase is relative in nature, which, in turn, renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

C) Claims 35 and 38 are indefinite in the recitation of "1E11, 1G2, 6G5, 10C5, 1G1, 6C1, 2E4, 7G2, 1F8, 4D1" because their characteristics are not known. The use of these laboratory designations as the sole means of identifying the claimed antibodies renders the claim indefinite because they are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines.

D) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

12. As pointed out previously and reiterated above, the priority of the instant claims is not clear; given that applicant has not provided documentary support for the written support/description of the instant claims and given that all of the priority documents have not been available to the examiner.

Given applicant's amended claims and assertions, filed 6/11/99 (Paper No. 16), that the following amended claims have a priority date of August 29/31 1990; the following rejection is set forth.
Again, applicant is requested to provide documentary support for the written support/description of the instant claims.

It is noted that for examination "human sequence immunoglobulin" reads on "humanized" or "recombinant" antibodies that have human sequences in them. Also, given that the genetic code is universal as well as both the homologies and polymorphisms of immunoglobulins; the recitation of "human sequence immunoglobulin" does not impart any particular human aspect to an immunoglobulin.

Although applicant does not address the 102(e) rejection directly; applicant's arguments, filed 6/11/99 (Paper No. 16), have been fully considered as to the nature and priority of the Queen et al. teaching, but are not found convincing essentially for the reasons of record.

Applicant's arguments are not found persuasive.

16. Claims 10, 12, 18-21, 31-34, 38-39, 41-49 are rejected under 35 U.S.C. § 103 as being unpatentable over Cobbold et al. (U.S. Patent No. 5,690,933) and Queen et al. (U.S. Patent No. 5,530,101) essentially for the reasons of record set forth in Paper No. 14 and those set forth herein. The instant claims are drawn to either antigen-specific or CD4-specific antibodies and cells that express said antibodies.

Applicant's arguments, filed 6/11/99 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant appears to assert a priority of 1993 for the claimed CD4-specific antibodies, nucleic acids and cells that express said CD4-specific antibodies/nucleic acids.

Applicant argues that the priority date of the prior art is after applicant's priority date; however the prior art is relying upon the 102(e) date of Cobbold et al. (U.S. Patent No. 5,690,933) and Queen et al. (U.S. Patent No. 5,530,101).

As pointed out above in section 3; applicant has not provided sufficient direction or objective evidence to provide for the written support for the current claims to these priority documents

Although applicant argues that the priority documents have priority; there is insufficient objective evidence that the priority documents have written description for these claims. Enablement and obviousness are not the standard for written description with respect to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

As pointed out above in section 12; it is noted that for examination "human sequence immunoglobulin" reads on "humanized" or "recombinant" antibodies that have human sequences in them. Also, given that the genetic code is universal as well as both the homologies and polymorphisms of immunoglobulins; the recitation of "human sequence immunoglobulin" does not impart any particular human aspect to an immunoglobulin.

Also, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Therefore, recitation of isolated cells from transgenic mice does not appear to obviate the obviousness of humanized antibodies in the prior art, including those that read on binding human CD4.

Queen et al. teach the use of known vectors and host cells encompassed by the claimed invention (e.g. CHO, myelomas, lymphocytes, with respect to the expression of humanized antibodies at the time the invention was made (see entire document, particularly columns 16-18).

Queen et al. teaches antibodies of 10^8 M^{-1} or stronger (e.g. see column 22).

Also, given the sequence homology of CD4 among primates; it would have been expected that antibodies that bound CD4 or an antigenic fragment thereof would have been expected to bind CD4 from other primates, in the absence of objective evidence to the contrary.

Applicant asserts that the claims drawn to human sequence immunoglobulins specific for human antigens are sufficiently enabled by priority application USSN 07/574,7748 and 07/575,962, filed 8/29/90 and 8/31/90, respectively.

It is noted that the 102(e) priority date(s) of Queen et al. precede applicant asserted priority date of is 1988 for generic antigen-specific antibodies (and cells expressing said antigen-specific antibodies).

Applicant further agues that Cobbold et al. does not exemplify human CD4-specific antibodies and that Queen et al. does not teach CD4 antibodies, nor fully human antibodies. In contrast to applicant's assertions, the prior art is not required to exemplify human CD4-specific antibodies. As pointed out previously, Cobbold et al. teach the generating antibodies to CD4 from different species including humans, antibodies that are derived from different species such as humans (see columns 2-3, overlapping paragraph for example). This reference differs from the claims by not exemplifying such human or humanized CD4-specific antibodies or cells that comprise said antibodies. Here, the combination of the prior art provided sufficient motivation and expectation of success in providing CD4-specific antibodies, including human antibodies as well as recombinant antibodies with human immunoglobulin sequences at the time the invention was made.

Also, it is noted the 102(e) priority date(s) of Cobbold et al. precedes the asserted priority date of the instant application to USSN 08/161,739, filed 12/3/93, for human CD4-specific antibodies (and cells expressing said CD4-specific antibodies.

Applicant's arguments concerning long-felt need are acknowledged, however mere arguments or conclusory statements do not provide sufficient evidence in view of the rejection of record.

As pointed out previously, it would have been prima obvious to one of ordinary skill in the art at the time the invention was made to generate either humanized to human CD4 or antigenic fragments thereof for various purposes, including therapeutic and diagnostic purposes. In addition, it would have been expected at the time the invention was made that certain antibodies that bound human CD4 would also bind other primate CD4, given the high sequence homology/identity among the primates at the time the invention was made. As pointed out previously and above; the recitation of a process limitation is not seen as further limiting the claimed product, as it is presumed that equivalent products can be obtained by multiple routes. The prior art provided expectation of success in deriving eukaryotic cells, including murine cells, to comprise recombinant or humanized immunoglobulins at the time the invention was made, as evidenced by Queen et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to select CD4-specific human and humanized antibodies as diagnostic and therapeutic agents at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
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Technology Center 1600
February 14, 2000
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